unfeasible and, in recent years, attention has been centered on cryoablation techniques.

Until recently, lack of a satisfactory working classification for acute retinopathy of prematurity has hampered understanding of the natural history of the disease, the risk factors for its progression and the efficacy of its treatment. The recently published *International Classification of Retinopathy of Prematurity* (ICROP) has led to the establishment of a randomized, prospective, controlled multicenter study of the safety and efficacy of ablative cryotherapy, permitting consistent identification of cases, enrollment at uniform stages of the disease and comparison of data from a large series of cases by observers at different locations. This protocol has recently been started under the auspices of the National Eye Institute (Multicenter Trial of Cryotherapy for Retinopathy of Prematurity) and, it is hoped, will answer many questions about this increasingly prevalent, potentially blinding disease of premature infants.

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REFERENCES

Patz A: Retrolental fibroplasia (retinopathy of prematurity) (Editorial). Am J Ophthalmol 1982 Oct; 94:552-554

The Committee for the Classification of Retinopathy of Prematurity: An international classification of retinopathy of prematurity. Arch Ophthalmol 1984 Aug; 102:1130-1134

Current Approach to Intractable Glaucoma

FILTERING OPERATIONS such as trabeculectomies and full-thickness scleral fistulizing procedures are currently used in the surgical management of glaucoma in patients who have failed to respond to maximal medical therapy and argon laser trabeculoplasties. These procedures will control the intraocular pressure in about 85% of patients with primary open-angle glaucomas. Unfortunately, the success rate of filtering procedures in patients with aphakic glaucomas, neovascular glaucomas, young patients and those with congenital glaucomas is poor, in most instances because the subconjunctival drainage area (bleb) is obliterated by scar tissue. In these patients, one method of modifying the healing process is the use of antimetabolites, such as 5-fluorouracil. A multicenter national trial is now studying the effectiveness of 5-fluorouracil as compared with the more traditional filtering operations in controlling intraocular pressure in these difficult-to-manage cases. 5-Fluorouracil (5 mg) is injected subconjunctivally 180° from the trabeculectomy site twice a day from day 1—the first day after the trabeculectomy—and then daily from day 8 to 14.

Another approach has been the use of setons. Certain types of setons allow the healing to progress naturally but limit contraction of the scar tissue as implantation of a solid plate acts to preserve a fluid reservoir. Scar tissue forms around the plate, but contraction of the scar tissue is restricted. Aqueous humor fills the cavity around the plate, forming a bleb, and percolates through the fibrous capsule to be absorbed by the surrounding vessels.

The principle of using a rigid device to maintain a bleb cavity in the region of the equator of the globe has been incorporated into the Schocket implant, the Krupin long tube valve and the Molteno implant. The Molteno implant consists of a long, thin silicone tube attached to a 13.5-mm diameter round, rigid methyl-methacrylate plate. The plate is sutured to the outer scleral surface in the equatorial region of the globe so that the large bleb that forms lies within the muscle cone beneath Tenon's capsule. The thin silicone tube attached to the plate is cut to the correct length and introduced into the anterior chamber. A transient rise in the intraocular pressure occurs two to ten weeks' postoperatively. Histologic studies suggest that this transient reaction is inflammatory in nature, and with resolution of the inflammation, intraocular pressure returns toward normal and remains well controlled with minimal medication. Short-term results have been encouraging, with 85% of patients maintaining intraocular pressure below 22 mm of mercury.

The major initial complication following introduction of the Molteno tube into the anterior chamber was short-term hypotony. This problem has been overcome, however, by placing an absorbable ligature around the tube (which opens spontaneously in about 75% of cases after four weeks) or by using a valve that opens at 8 to 10 mm of mercury, as used by Krupin.

The current surgical approach to severe, intractable glaucoma by either trabeculectomy, 5-fluorouracil injections or implantation of setons that incorporate equatorial plates to maintain a bleb cavity has significantly increased the success rates in these difficult management cases.

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REFERENCES

Molteno AC, Ancker E, Van Biljon G: Surgical technique for advanced juvenile glaucoma. Arch Ophthalmol 1984 Jan; 102:51-57

Schocket SS, Lakhanpal V, Richards RD: Anterior chamber tube shunt to an encircling band in the treatment of neovascular glaucoma. Ophthalmology 1982 Oct; 89:1188-1194

Ultraviolet Filtration and Light Damage

THE HUMAN LENS absorbs ultraviolet and deep blue light, and there is evidence that some of this energy alters proteins whose structure is critical to the transparency of the tissue. Over a lifetime, this process contributes to yellowing and hardening of the lens that, in extreme cases, becomes dense enough to interfere with vision and to be called a cataract.

Light that passes through the lens is absorbed in the retina and in the retinal pigment epithelium, a supportive tissue that functions, among other things, to phagocytize retinal waste products. This energy facilitates the formation of oxidative free radicals that damage the complex lipid membranes of the photoreceptors. These oxidized lipids are relatively indigestible and hasten the accumulation of lipid debris that clogs the retinal pigment epithelium of older eyes. In some eyes the overburdened retinal pigment epithelium breaks down, with resultant damage to the adjacent retina. This process appears to be a major factor in the development of age-related macular degeneration.

Very bright or sustained light exposure can also be damaging in the short term to photoreceptors and retinal pigment epithelium. Spending the day on a sunny beach or ski slope without sunglasses may be enough to cause a degree of cellular injury—and, the longer the exposure, the less easy it is for the visual cells to recover. The most damaging wavelengths for photic injury to the retina are in the ultraviolet and the blue end of the visible spectrum.

On the basis of these findings, the use of good-quality

ultraviolet-absorbing sunglasses under bright outdoor conditions seems prudent. It also seems prudent to provide some extra ultraviolet filtration for people who have had their lens removed by cataract surgery. Manufacturers have responded to the latter concerns by marketing spectacles and intraocular lenses that block all light below 400 nm (the cutoff for a human lens). Unfortunately, the manufacturers of sunglasses have not been so explicit about the characteristics of their products. Ordinary glass and plastic absorb the far ultraviolet (below 350 nm) and some manufacturers advertise such lenses as "UV absorbing," which is misleading because light between 350 and 450 nm may still be transmitted and may be damaging.

To purchase sunglasses for ultraviolet protection, I suggest asking the vendor for information about spectral characteristics. An effective sunglass for retinal protection should block not only the full range of ultraviolet, but also the deep blue end of the spectrum. Because of the reduction in blue light transmission, such glasses often have a yellowish or amber tint in addition to whatever degree of darkness they may have.

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REFERENCES

Lerman S: Radiant Energy and the Eye. New York, Macmillan, 1980

Sliney DH: Eye protective techniques for bright light. Ophthalmology 1983 Aug; 90:937-944

Recessive Human Cancer Genes

RECENT OBSERVATIONS in retinoblastoma, a relatively rare malignant intraocular tumor in childhood, have provided evidence for a new class of human cancer genes. It is generally accepted that division and differentiation of cells in higher organisms are regulated by many controls and that tumors arise through the accumulation of several changes releasing the cells from constraints on growth. Statistical data suggest that two successive mutationlike changes are required for the development of retinoblastoma, three to four for leukemias and six to seven for carcinomas.

The first evidence for the presence of recessive cancer genes in humans was provided by retinoblastoma. It has been known for more than 15 years that in 2% to 3% of retinoblastoma cases, a loss or deletion of region q14 of chromosome 13 was associated with the appearance of retinoblastoma. Observations that the loss or deletion of both 13 chromosomes had occurred in the tumor of one patient suggested that the two "mutations" postulated by Knudson as being necessary for retinoblastoma to develop might be the loss or inactivation of both copies of a recessive gene on chromosome 13 perhaps necessary for differentiation. This concept has been strengthened by the subsequent observation that in nearly 80% of all retinoblastomas examined, both sporadic and familial, chromosome 13 becomes homozygous, presumably for the mutant or abnormal regulator gene at the retinoblastoma locus. Recently osteosarcoma, a tumor known to occur frequently in families with retinoblastoma, has been shown to be homozygous for the same 13 chromosome, suggesting that this "regulator gene" may normally limit bone as well as retinal growth.

The recessive "regulatory" gene model in humans has subsequently been shown to hold for Wilms' tumor where loss of both copies of a recessive cancer gene on the short arm of chromosome 11 has been found. This same locus seems to be involved as well in some other childhood tumors, specifically rhabdomyosarcoma and hepatoblastoma.

It is not surprising that the childhood tumors arise from relatively fewer events than adult tumors because they appear earlier in life. It is clear from the experience with retinoblastoma that specific DNA changes, whether inherited or not, are inherently a part of the tumorigenic process.

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REFERENCES

Benedict WF, Murphree AL, Banerjee A, et al: Patient with 13 chromosome deletion: Evidence that the retinoblastoma gene is a recessive cancer gene. Science 1983 Feb 25; 219:973-975

Cavenee WK, Dryja TP, Phillips RA, et al: Expression of recessive alleles by chromosomal mechanisms in retinoblastoma. Nature 1983 Oct 27-Nov 2; 305:779-784

Klein G, Klein E: Evolution of tumours and the impact of molecular oncology. Nature 1985 May 16-22; 315:190-195

Koufos A, Hansen MF, Copeland NG, et al: Loss of heterozygosity in three embryonal tumours suggests a common pathogenetic mechanism. Nature 1985 Jul 25-31; 316:330-334

Murphree AL, Benedict WF: Retinoblastoma: Clues to human oncogenesis. Science 1984 Mar 9; 223:1028-1033

Diabetic Macular Edema

MACULAR EDEMA (swelling of the central, reading part of the retina) is the leading cause of vision loss in the diabetic population. Although this vision loss is usually not as severe as that caused by bleeding inside the eye, patients with this complication can lose reading and driving vision. Depending on a patient's age at diagnosis of diabetes, one population-based study found the prevalence rate of macular edema to vary from 0% to 3% in those patients with diabetes for less than 5 years and 28% to 29% for those patients with diabetes for 20 or more years. A recently published national collaborative study has shown that photocoagulation is an effective treatment for many of these patients.

The beneficial effect of photocoagulation treatment was shown in those eyes with early diabetic retinopathy (scattered retinal hemorrhages, microaneurysms and exudates) and clinically significant macular edema. Clinically significant macular edema is defined as:

- thickening of the retina at or within 500 microns of the center of the macula (located one disc diameter temporal to the optic nerve),
- hard exudates at or within 500 microns of the center of the macula if associated with thickening of adjacent retina and
- a zone or zones of retinal thickening one disc area or larger in size, any part of which is within one disc diameter of the center of the macula.

Thus, diabetic patients with early diabetic retinopathy and one or more of the above findings should be considered for focal or limited-scatter photocoagulation treatment of the macula. Whether to treat macular edema in eyes with more advanced retinopathy (venous dilatation and beading, intraretinal microvascular abnormalities, cotton wool spots or retinal or disc neovascularization) was left to the discretion of the treating ophthalmologist. The study showed a beneficial trend of treatment in these eyes, but the results were not conclusive. Panretinal photocoagulation treatment should be applied if a high-risk characteristic is present as defined in a prior national collaborative study.